REMARKS

Preliminary Amendments

With the entry of the preliminary amendments herein, claims 2-6, 11, 13-20, 25, 28-86 are pending in the application. New claims 38-86 have been added to this application and have basis in the claims from which they depend. Claims 2, 3, 5, 13, 19, 36 and 37 have been amended. Claim 3 and 13 have been amended to correct typographical errors in the body of the claims. Claims 2, 5, 19, 36 and 37 have been amended to correct a typographical error in the bonds of formula (I). Applicants submit that no new matter has been added by these amendments.

Response to Restriction Requirement

The Examiner has required restriction to one of two groups of claims, with the claims in Group II (claims 15, 16, 19-20, 25, 36 and 37) being drawn to compounds and compositions; and Group I (claims 2-6, 11, 13, 14, 17, 18 and 28-35) being drawn to various methods of treating diseases with compounds and compositions of Group II. The Office Action states that restriction to one of these two claim groups is necessary as the aforementioned claim groups are distinct from each other. It appears that the Examiner is making a distinction between claims directed at methods as opposed to claims directed at compositions of the present application. In this light, it should be noted that claim 18 of Group I is a composition claim dependent from claim 15 of Group II. Applicants presume that the inclusion of claim 18 in Group I was an error on the part of the Examiner.

In response to the above-noted restriction requirement, applicants hereby elect the claims of Group I. (i.e. claims 2-6, 11, 13, 14, 17, 28-35 and newly added claims 38-86) with traverse.

The applicants hereby traverse the restriction requirement in its entirety. Restriction is only proper where "two or more independent and distinct inventions are claimed in one application" (35 U.S.C. § 121). Applicants respectfully submit that the two groups of claims

identified by the Examiner are not directed to "independent and distinct inventions", but to different embodiments of the same invention. The present invention provides 24-hydroxyvitamin D compounds and methods of using these compounds for treating or preventing various conditions.

In one embodiment, the invention provides 24-hydroxyvitamin D compounds. In another embodiment, the invention provides using these compounds to treat or prevent various conditions. It should be clear from the disclosure of the invention that the 24-hydroxyvitamin D or 24 hydroxy*pre*vitamin D compounds are an essential component of each and every embodiment of the present invention. Applicants submit that the claims of Group I and II are therefore not directed to separate and distinct inventions but to the same invention. Thus, restriction of any of the groups of the claims is improper under 35 U.S.C. § 121.

Applicants submit furthermore that even if the claim groups were directed to independent or distinct inventions, rather than two embodiments of the same invention, restriction would not be appropriate in this case for the following reasons. The Manual of Patent Examining Procedure ("MPEP") states that

> "If the search and the examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to distinct or independent inventions." MPEP § 803

Applicants respectfully submit that all claims of the present invention could be examined together without placing any serious burden on the United States Patent and Trademark Office. The claims of Groups I and II are so inextricably related to one another that, for the sake of efficiency, they should be examined in the same application. All the claims of the present application are directed to 24-hydroxyvitamin D or 24 hydroxy*pre*vitamin D compounds and methods of using such compounds. A complete search

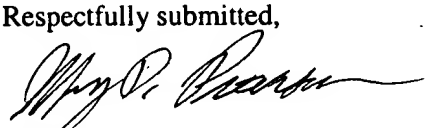
of the prior art relating to these 24-hydroxyvitamin D and 24 hydroxy*pre*vitamin D compounds would necessarily require a search of the subject matter of both groups. Given the close relationship between the claims of Groups I and II, prosecution of the claims in the same application would be administratively efficient by the Patent Office. Specifically, by prosecuting the applications together, the searches could be consolidated, and one Examiner could readily examine the subject matter of all the claims of the application at once.

Applicants therefore traverse the restriction requirements for the reasons set forth above.

Summary

Applicants respectfully submit that claims 2-6, 11, 13-20, 25, 28-86 are in condition for allowance and respectfully solicit an early notice of allowance. In the event that there are any issues that can be expedited by telephone conference, the examiner is invited to telephone the undersigned at the number indicated below.

Respectfully submitted,

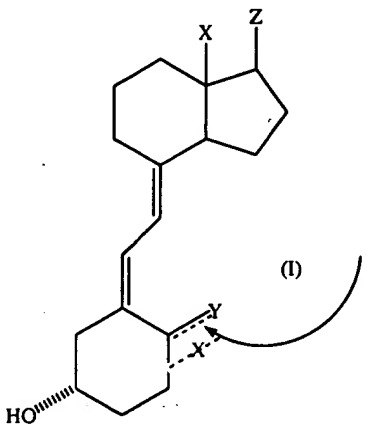


Jeffrey D. Peterson
Reg. No. 49,038

Docket No.: 17620/9316
Michael Best & Friedrich LLP
One South Pinckney Street
P. O. Box 1806
Madison, WI 53701-1806
(608) 257-3501

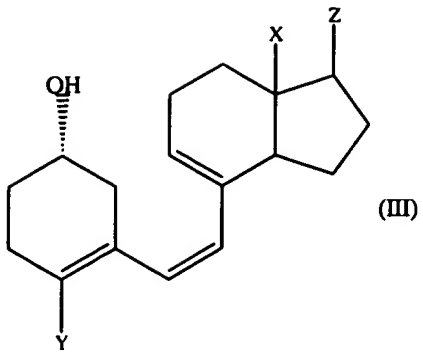
VERSION WITH MARKINGS TO SHOW CHANGES MADE

2. (Twice Amended) A method of achieving an effect in a patient comprising administering an effective amount of a vitamin D compound which is a 24-hydroxyvitamin D compound wherein the effect is treating or preventing bone loss or bone mineral content, hyperparathyroidism, hyperproliferation, or modulating the immune or inflammatory response, and wherein said 24-hydroxyvitamin D is a compound of formula (I):



wherein Z represents a saturated or unsaturated, substituted or unsubstituted, straight-chain or branched C_4 - C_{18} hydrocarbon group in which the C-24 or equivalent position is hydroxylated; Y is a methylene group if Y is double bonded to the A-ring or a methyl group or hydrogen if Y is single bonded; and X is hydrogen, lower alkyl or lower fluoroalkyl.

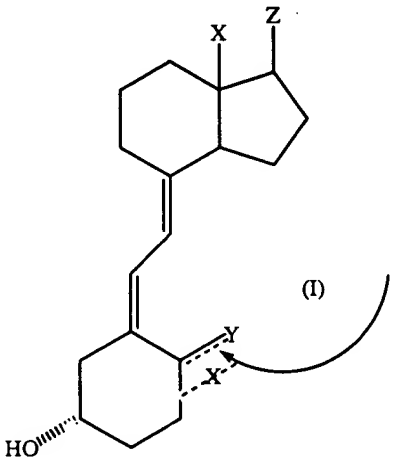
3. (Twice Amended) A method of achieving an effect in a patient comprising administering an effective amount of a vitamin D compound which is a 24-hydroxy*pre*vitamin D, wherein the effect is treating or preventing bone loss or bone mineral content, hyperparathyroidism, hyperproliferation, or modulating the immune and inflammatory responses, wherein said 24-hydroxy*pre*vitamin [24-hydroxyprevitamin] D is a compound of formula (III):



(III)

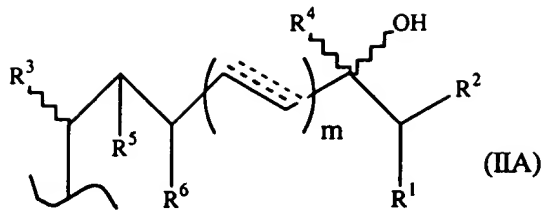
wherein Z represents a saturated or unsaturated, substituted or unsubstituted, straight-chain or branched C_4 - C_{18} hydrocarbon group in which the C-24 or equivalent position is hydroxylated; Y is a methyl group or hydrogen; and X is hydrogen, lower alkyl or lower fluoroalkyl.

4. (Three times Amended) The method of claim 14 wherein said 24-hydroxyvitamin D is a compound of formula (I):



(I)

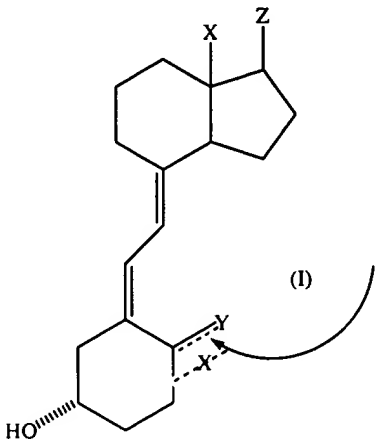
wherein Y is a methylene group if Y is double bonded to the A-ring or a methyl group or hydrogen if Y is single bonded; and X is hydrogen, lower alkyl or lower fluoroalkyl; and Z is a side chain of formula (IIA):



(IIA)

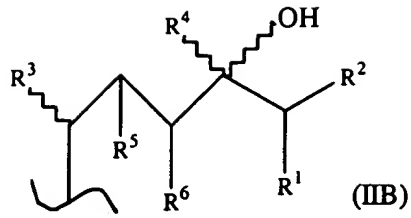
wherein a dotted line along the side chain represents an optional additional C-C bond and m is 0 or 1; R^1 and R^2 are independently lower alkyl, lower fluoroalkyl, lower alkenyl, lower fluoroalkenyl, lower cycloalkyl or, taken together with the carbon to which they are bonded, form a C_3-C_8 cyclohydrocarbon ring; R^3 is hydrogen, lower alkyl, lower fluoroalkyl, lower alkenyl or lower fluoroalkenyl; R^4 is lower alkyl, lower fluoroalkyl, lower alkenyl or lower fluoroalkenyl; and R^5 and R^6 are each hydrogen or taken together form a double bond between C-22 and C-23.

5. (Three Times Amended) The method of claim 14 wherein said 24-hydroxyvitamin D is a compound of formula (I):



(I)

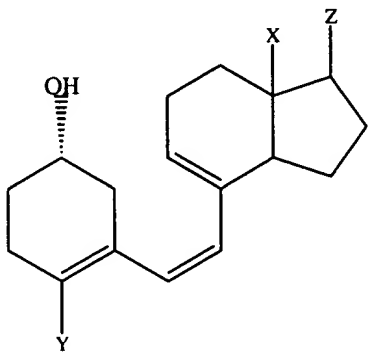
wherein Y is a methylene group if Y is double bonded to the A-ring or a methyl group or hydrogen if Y is single bonded; and X is hydrogen, lower alkyl or lower fluoroalkyl; and Z is a side chain of formula (IIB):



(IIB)

wherein R^5 and R^6 are each hydrogen or taken together form a double bond between C-22 and C-23, R^3 is hydrogen, lower alkyl, lower fluoroalkyl, lower alkenyl or lower fluoroalkenyl; R^4 is lower alkyl, lower fluoroalkyl, lower alkenyl or lower fluoroalkenyl; and R^1 and R^2 are independently hydrogen, lower alkyl, lower fluoroalkyl, lower alkenyl, lower fluoroalkenyl, lower cycloalkyl or taken together with the carbon to which they are bonded form a C_3-C_8 cyclocarbon ring.

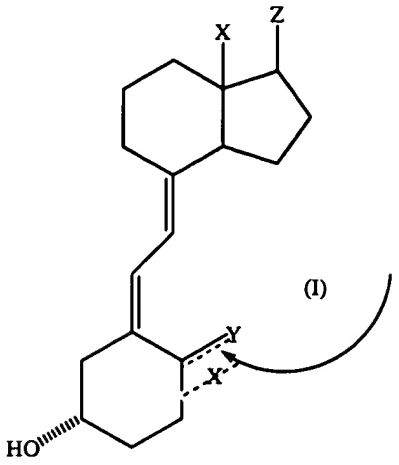
13. (Twice Amended) A method of achieving an effect in a patient comprising administering an effective amount of a vitamin D compound which is a 24-hydroxy*pre*vitamin D wherein the effect is increasing or maintaining bone mass or bone mineral content, lowering or maintaining lowered parathyroid hormone level, inhibiting hyperproliferative effects, inducing or enhancing cell differentiation, modulating immune response, or modulating inflammatory response, wherein said 24-hydroxy*pre*vitamin D is a compound of formula (III):



(III)

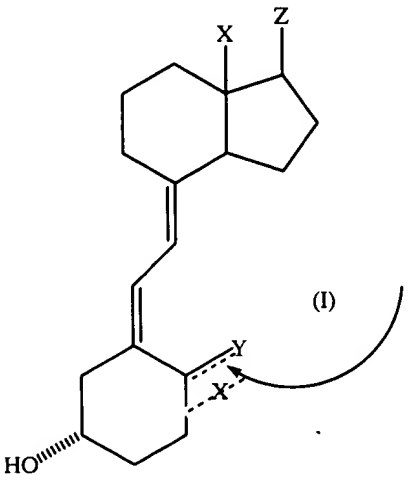
wherein Z represents a saturated or unsaturated, substituted or unsubstituted, straight-chain or branched C_4 - C_{18} hydrocarbon group in which the C-24 or equivalent position is hydroxylated; Y is a methyl group or hydrogen; and X is hydrogen, lower alkyl or lower fluoroalkyl.

19. (Once Amended) A 24-hydroxyvitamin D compound which is a compound of formula (I):

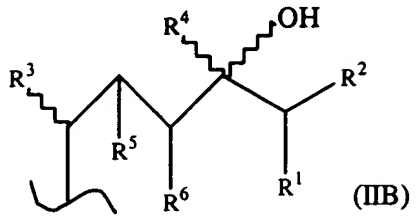


wherein Z represents a saturated or unsaturated, substituted or unsubstituted, straight-chain or branched C_4 - C_{18} hydrocarbon group in which the C-24 or equivalent position is hydroxylated; Y is a methylene group if Y is double bonded to the A-ring or a methyl group or hydrogen if Y is single bonded provided that the compound of formula (I) is not 24-hydroxyvitamin D_2; and X is hydrogen, lower alkyl or lower fluoroalkyl provided that the compound of formula (I) is not 24-hydroxyvitamin D_2.

36. (Twice Amended) The composition of claim 15, wherein said 24-hydroxyvitamin D is a vitamin D_2 compound of formula (I):



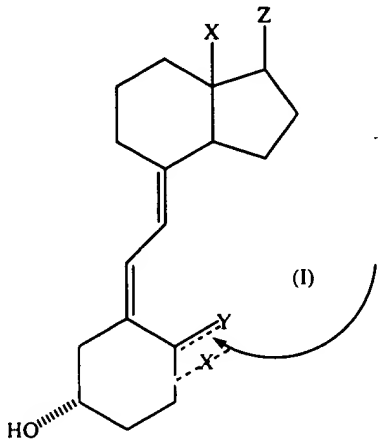
wherein Y is a methylene group if Y is double bonded to the A-ring or a methyl group or hydrogen if Y is single bonded; and X is hydrogen, lower alkyl or lower fluoroalkyl; and wherein Z is a sidechain of formula (IIB):



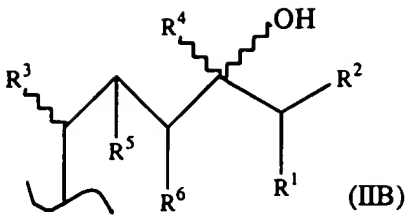
(IIB)

wherein R^5 and R^6 are each hydrogen or taken together form a double bond between C-22 and C-23, R^3 is hydrogen, lower alkyl, lower fluoroalkyl, lower alkenyl or lower fluoroalkenyl; R^4 is lower alkyl, lower fluoroalkyl, lower alkenyl or lower fluoroalkenyl; and wherein R^1 is a methyl group, and wherein R^2 is a methyl group.

37. (Twice Amended) The tablet of claim 25, wherein the vitamin D compound is a vitamin D_2 compound of formula (I):



wherein Y is a methylene group if Y is double bonded to the A-ring or a methyl group or hydrogen if Y is single bonded; and X is hydrogen; and wherein Z is a sidechain of formula (IIB):



(IIB)

wherein R^5 and R^6 are each hydrogen or taken together form a double bond between C-22 and C-23, R^3 is hydrogen, lower alkyl, lower fluoroalkyl, lower alkenyl or lower fluoroalkenyl; R^4 is lower alkyl, lower fluoroalkyl, lower alkenyl or lower fluoroalkenyl; and wherein R^1 is a methyl group, and wherein R^2 is a methyl group.